

REGISTRY OF RADIOACTIVE SEALED SOURCES AND DEVICES  
SAFETY EVALUATION OF SEALED SOURCE  
(AMENDED IN ITS ENTIRETY)

NO: NR-1081-S-101-S

DATE: March 22, 2004

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SOURCE TYPE: Therapeutic Seed Source

MODEL: I-125 SL, I-125 SH, and Pd-103 SL

MANUFACTURER/DISTRIBUTOR: Mills Biopharmaceuticals, Inc.  
120 N.E. 26<sup>th</sup> Street  
Oklahoma City, Oklahoma 73105

ISOTOPE:

MAXIMUM ACTIVITY:

Iodine-125

5.55 GBq (150 millicuries)

Palladium-103

**111 MBq (3 millicuries)**

LEAK TEST FREQUENCY:

6 months

PRINCIPAL USE:

(V) General Medical Use  
**For use in manual brachytherapy  
in accordance with 10 CFR 35.400  
or equivalent Agreement State  
regulations**

CUSTOM SOURCE:

\_\_\_\_ YES     X  NO

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SOURCE TYPE: Therapeutic Seed Source

DESCRIPTION:

The Mills Biopharmaceuticals, Inc. (MBI) Model I-125 SL and I-125 SH seeds contain sodium iodine-125 absorbed on solid silver spheres and encapsulated in a cylindrical titanium capsule. As indicated in Attachment 1, the core of the silver seed is a 0.5 mm  $\pm$  0.05mm (0.017"  $\pm$  0.0017") sphere. Each MBI I-125 seed's maximum external dimensions are 4.5 mm (0.177")  $\pm$  0.3mm (0.0188") in length and 0.80 mm (0.0315")  $\pm$  0.1 mm (0.0004") in diameter. The cylindrical metal casing is A-40 (commercially pure) titanium, conforming to ASTM F-67-95, with a wall thickness of 0.05 mm (0.0020")  $\pm$  0.01 mm (0.0004"). The titanium tubing is welded on one end, inverted, the spheres added, and the open end closed with a weld. The welds are made in a vertical position in the presence of a gentle flow of high purity argon to consistently achieve good quality high strength welds.

Both models contain five silver spheres. The Model I-125 SH contains a maximum activity of 150 mCi (5.55 GBq) and the Model I-125 SL contains a maximum activity of 1 mCi (37 MBq). The two models differ only in total radioactivity contained.

**The Model Pd-103 SL seeds have palladium-103 absorbed on the two silver spheres at the ends of the seeds, while the three spheres in the middle remain non-radioactive. The titanium tubing is welded on one end, inverted, five spheres added in a 1 hot - 3 cold - 1 hot configuration, and the open end closed with a weld. Physical dimensions and mechanical construction of both the silver spheres and the titanium casing of the Model Pd-103 SL seeds are identical to those of the iodine seeds as described above. The Model Pd-103 SL contains a maximum activity of 111 MBq (3.00 mCi). The Model Pd-103 SH will no longer be distributed by the manufacturer.**

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LABELING:

The physical size of the individual seed prevents direct labeling of the individual sources. The seeds are supplied as a group of seeds with an activity within a stated range on the assay date and are packaged in a one-dram vial. Each production lot is assigned a unique lot number. A label is affixed to the vial stating: "Caution - Radioactive Materials," distributor name, isotope, activity range, total activity, assay date, and the trefoil radiation symbol. An additional label is attached to the lead storage container which includes: a "Caution - Radioactive Material" statement, the trefoil radiation symbol, product description, activity range, total activity, number of seeds, assay date, lot number, instructions to see the package insert and a warning against distribution to unauthorized persons. The labels will comply with the provisions of 10 CFR 32.74, 20.1901, and 20.1904. The labels will be legible and made of durable material.

DIAGRAMS:

See Attachments 1, 2 and 3.

CONDITIONS OF NORMAL USE:

The Mills Biopharmaceuticals, Inc. **Models I-125 SL, I-125 SH, and Pd-103 SL** brachytherapy seeds are designed for use in the interstitial treatment of cancerous tumors. The placement of iodine-125 and palladium-103 brachytherapy seeds in tissue under surgical conditions is assisted by the use of any one of several implant tools commercially available. In addition, **all three models** are designed to be sterilized using ethylene oxide or autoclaves at normal autoclave temperature and pressure variations up to 138° C (280° F) and 35 psi (241.3 kPa). The titanium encapsulation should not be exposed to concentrated acids **nor** sterilized by dry heat methods. Due to the high dose rates from the sources, appropriate handling equipment, such as forceps, must be used. Ruptured, leaky or damaged sources should never be used.

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SOURCE TYPE: Therapeutic Seed Source

PROTOTYPE TESTING:

The iodine-125 brachytherapy seed prototypes were subjected to tests to demonstrate that the sources will maintain their integrity under stresses of use and accidents that may occur. These tests included temperature, impact, percussion, autoclave temperatures and pressures for sources with wall thickness of 0.05 mm (0.00197").

The tests performed closely followed the recommendations of ANSI N44.1-1973. The only deviations from the standard's recommendations were an autoclave high temperature and limitations imposed on the minimum diameter requirements of the source tube. The manufacturer indicated the sources passed each of these tests.

The **Model Pd-103 SL** brachytherapy seeds are constructed with identical materials and identical fabrication methods to those of the iodine-125 seeds. The manufacturer reported that the seeds are identical except for the radionuclide and, therefore, the prototype tests conducted with the iodine-125 models as described above are applicable to the palladium-103 models.

EXTERNAL RADIATION LEVELS:

Calculated radiation levels using gamma radiation constants provided in the Radiological Health Handbook are tabulated below. The value provided for I-125 is given as approximately 0.7 Rcm<sup>2</sup>/hr/mCi. Containment of 1.0 mCi within a welded titanium capsule with corresponding wall thickness of 0.05 mm (0.0020") would attenuate the output by approximately 15%.

	1.97" (5 cm)	3.94" (10 cm)	11.8" (30 cm)
Unencapsulated:	28 mR/hr	7 mR/hr	0.8 mR/hr
Encapsulated:	24 mR/hr	6 mR/hr	0.7 mR/hr

Radiation levels for a maximum loading would be proportionately higher.

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EXTERNAL RADIATION LEVELS (cont'd):

The manufacturer reported that the radiation profiles for the **Model Pd-103 SL** will be less than the **Models I-125 SH and I-125 SL** of similar activity based upon the lower specific gamma radiation constant of  $6.219 \times 10^{-5}$  (mSv/h)/MBq at 100cm for the **Model Pd-103 SL** versus  $7.432 \times 10^{-5}$  (mSv/h)/MBq at 100cm for **Models I-125 SH and I-125 SL** and an estimated Pd-103 attenuation of 55% for 0.05 mm (0.020") of titanium.

QUALITY ASSURANCE AND CONTROL:

Sources manufactured by Mills Biopharmaceuticals, Inc. are governed by its quality policy manual. A copy of the program is on file with NRC. The QC program contains provisions for design and procurement documentation reviews and includes elements for ensuring identity of incoming products, conducting receipt inspection, initial leak tests, autoclave and second leak tests, **and** inspection of assembly and welds.

The manufacturer conducts the leak tests in accordance with ANSI N44.2-1973, Section A1.3. Any source found with more than 0.005  $\mu$ Ci (185 Bq) of removable contamination is rejected and relocated in locations away from the production and assembly areas.

LIMITATIONS AND OTHER CONSIDERATIONS OF USE:

1. These sources shall be distributed to specific licensees of the U.S. Nuclear Regulatory Commission or an Agreement State. **The medical use of these sources is regulated under 10 CFR 35.400 or equivalent Agreement State regulations.**
2. These sources shall be tested for leakage at time intervals not to exceed 6 months. Leak testing shall be governed by individual license requirements from the U.S. Nuclear Regulatory Commission or an Agreement State.
3. Sources should not be exposed to temperatures in excess of 138° C (280.4° F) and pressures in excess of 35 psi (241.3 kPa).

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LIMITATIONS AND OTHER CONSIDERATIONS OF USE (cont'd):

4. Due to the high surface dose rates exhibited by these sources when unshielded, sources should be stored in the shielded container supplied with each source or set of sources.
5. The sources shall not be autoclaved in plastic tubing or plastic containers. Only autoclave in suitable materials such as stainless steel, glass, nylon, teflon, or tin should be used. The sources shall not be exposed to concentrated acids or alkaline fluids or sterilized by dry heat methods. These sources are designed for use in controlled laboratory or medical surgery conditions and should not be subjected to conditions exceeding those specified by the ANSI rating 77C64221 classification.
6. Handling, storage, use, transfer and disposal: To be determined by the licensing authority.
7. This registration sheet and the information contained within the references shall not be changed without the written consent of the U.S. Nuclear Regulatory Commission.
8. Reviewer Note: Please ensure the safety procedures outlined in 10 CFR **35.400 or equivalent Agreement State regulations** are adhered to, especially as they pertain to the handling of the sources.

SAFETY ANALYSIS SUMMARY:

Based on our review of the information and test data cited below and the past history of similar source design, we conclude that MBI Models I-125 SH, I-125 SL, **and Pd-103 SL** are acceptable for licensing purposes.

Furthermore we continue to conclude that these sources would be expected to maintain their containment integrity for normal and accidental conditions for use which might occur during the uses specified in this certificate.

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SAFETY ANALYSIS SUMMARY (cont'd):

The United States Food and Drug Administration (FDA) **granted Mills Biopharmaceuticals, Inc., authorization to market the iodine-125 therapeutic seeds** (FDA letter dated April 16, 1999, Reference K984446). The United States Food and Drug Administration (FDA) **granted Mills Biopharmaceuticals, Inc., authorization to market the palladium-103 therapeutic seeds** (FDA letter dated August 31, 2001, Reference K011427).

REFERENCES:

The following supporting documents for the Mills Biopharmaceuticals Inc. Models I-125 SH, I-125 SL, Pd-103 SL and Pd-103 SH brachytherapy sealed sources are hereby incorporated by reference and are made part of this registration document.

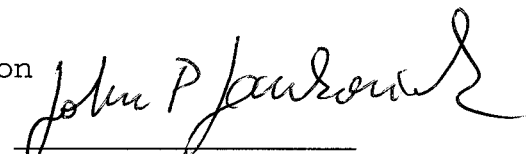
- Mills Biopharmaceuticals, Inc., letters dated June 13, 1999, October 01, 1999, and November 12, 1999, with enclosures thereto.
- Mills Biopharmaceuticals, Inc., letters dated April 30, 2001, June 29, 2001, September 14, 2001, with enclosures thereto, and electronic mail dated September 18, 2001.
- **Mills Biopharmaceuticals, Inc., letter dated October 24, 2003, with enclosures thereto, two electronic mails dated March 4, 2004, and two electronic mails dated March 16, 2004.**

ISSUING AGENCY:

United States Nuclear Regulatory Commission


Date: March 22, 2004

Reviewer:

  
John P. Jankovich

Date: March 22, 2004

Concurrence:

  
Ujagar S. Bhachu

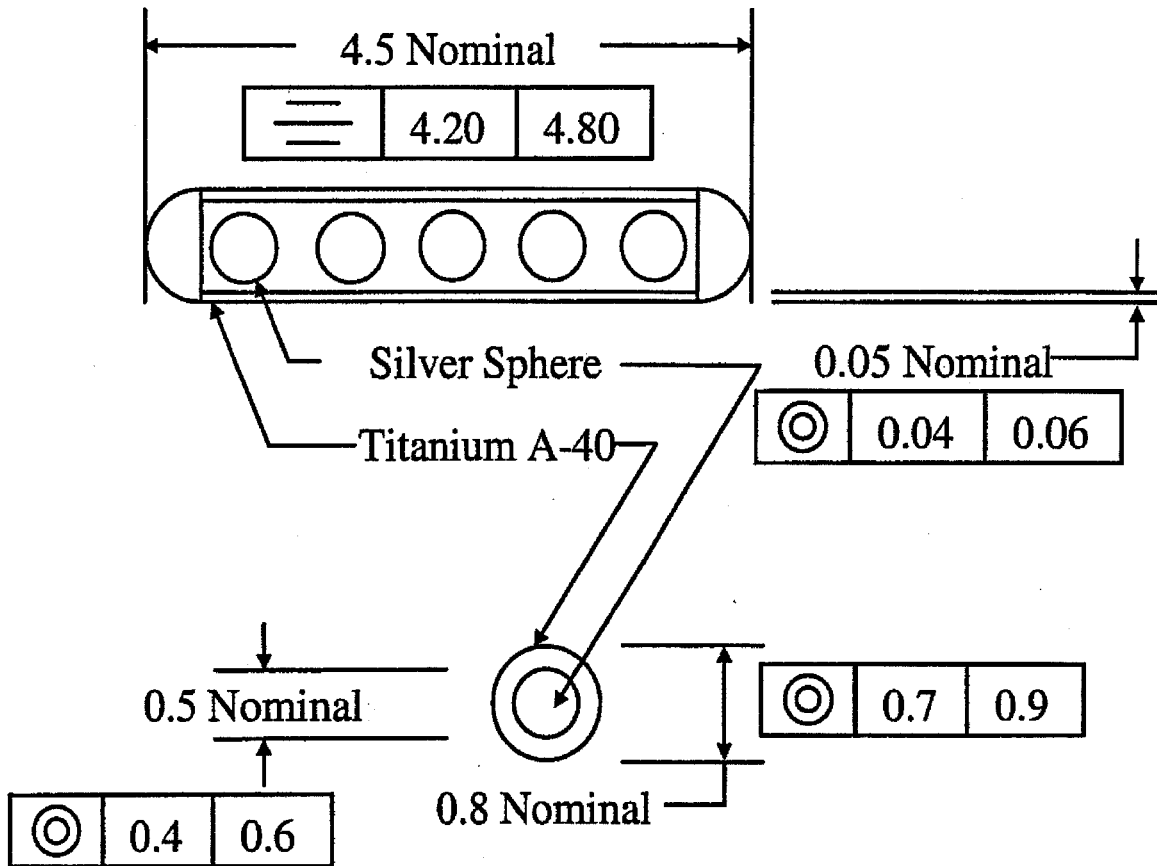
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Attachment 1

SOURCE TYPE: Therapeutic Seed Source



Seed Construction  
 (Dimensions in millimeters)



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Attachment 2

SOURCE TYPE: Therapeutic Seed Source


<b>ProstaSeed</b> Model 125SL	
I-125 Source	
Mills Biopharmaceuticals, Inc. OKC, OK	
Total activity:	MBq
Total #:	
Apparent activity range:	MBq
Assay date:	12:00 CST
Lot #:	
0016439	08259901

 Caution  
Radioactive  
Material

**CAUTION: Federal (U.S.A.) law prohibits dispensing without prescription. Read package insert.**

Lead Container Label for I-125 seeds  
Label Dimensions: 1.5 x 3.25 inch (3.81 x 8.25 cm)

<b>ProstaSeed</b> Model 125SL	
I-125 Source	
Mills Biopharmaceuticals, Inc. OKC, OK	
Total activity:	MBq
Total #:	
Apparent activity range:	MBq
Assay date:	12:00 CST
Lot #:	
0016439	08259901

 Caution  
Radioactive  
Material

**CAUTION: Federal (U.S.A.) law prohibits dispensing without prescription. Read package insert.**

Vial Label for I-125 seeds  
Label Dimensions: 1.12 x 1.87 inch (2.84 x 4.75 cm)

All shipments of sources and containers will include storage, receiving and handling instructions.


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Attachment 3

SOURCE TYPE: Therapeutic Seed Source

<b>MBI Pd-103 Brachytherapy Seed Model 103SL</b>	
<b>Pd-103 Source</b>	
<b>Mills Biopharmaceuticals, Inc. OKC, OK</b>	
Total activity: XXXX.XX MBq	 Caution Radioactive Material  <b>CAUTION: Federal (U.S.A.) law prohibits dispensing without prescription. Read package insert.</b>
Total #: XXX	
Apparent activity range: XX.XXX - XX.XXX MBq	
Assay date: XX/XX/XXX 12:00 CST	
Lot #: XXXXXX	
0000047	500053 Rev. A

Lead Container Label for Pd-103 seeds  
Label Dimensions: 1.5 x 3.25 inch (3.81 x 8.25 cm)

<b>MBI Pd-103 Brachytherapy Seed</b>	Model 103SL Pd-103 Source
<b>Mills Biopharmaceuticals, Inc. OKC, OK</b>	 Caution Radioactive Material  <b>CAUTION: Federal (U.S.A.) law prohibits dispensing without prescription. Read package insert.</b>
Total activity: XXXX.XXX MBq	
Total #: XXX	
Apparent activity range: XX.XXX - XX.XXX MBq	
Assay date: XX/XX/XXXX 12:00 CST	
Lot #: XXXXXX	500053 Rev. A

Vial Label for Pd-103 seeds  
Label Dimensions: 1.12 x 1.87 inch (2.84 x 4.75 cm)